POTASSIUM IODIDE IN THE TREATMENT OF SYPHILIS*

BY

P. KEEN

Non-European Hospital, Johannesburg, Union of S. Africa

Since the advent of the recognized antispirochaetal agents, the use of iodides has diminished and they are regarded by many as obsolete in the treatment of syphilis.

McDermott (1947) gives the following summary :

Potassium iodide is not an antispirochaetal agent, and hence has no value in the treatment of early syphilis. Whether the drug exerts an effect upon the healing of lesions of late syphilis has never been established with certainty, but generations of clinical observers believed that such an effect was demonstrable. The controversy is no longer of importance, as the arsenicals and penicillin are so effective in the treatment of the gummatous lesions of late syphilis. Occasionally potassium iodide appears to be of value in relieving the pain caused by diminished coronary arterial circulation secondary to syphilitic atresia of the coronary orifices. If such an action exists, it is presumably exerted through a mechanism other than a direct effect upon the syphilitic lesions.

Moore (1941) states :

The use of iodides in the treatment of syphilis rests purely on clinical and empirical grounds. The exact evaluation of the worth of the iodides in modern syphilotherapy, combined, as they must be, with other more powerful antisyphilitic drugs, is to our way of thinking impossible. It may well be that aside from their effect in accelerating the healing of outspoken late lesions, they have no influence of any kind on the ultimate outcome, measured in terms of "cure" or arrest. Indeed, in early syphilis, we are inclined to think that this is probably the case, and that patients treated with an arsenical and a heavy metal alone do quite as well as those to whom iodides are also given. However, their undoubted healing power in late syphilis and the theoretical consideration that they aid in the destruction of treponemes by enhancing the penetrating powers of other drugs are considerations too alluring to pass by ; and we share the general feeling that they still have a place, even if a humble one, in the management of most patients with syphilis.

Greenbaum and Cobane (1934) state not only that iodine and the iodides may be dispensed with in the treatment of syphilis but that the fibrolytic

effects ascribed to these agents are obtained more rapidly and more certainly by the arsenical and bismuth preparations. These authors contend that when the iodides are exhibited in cases of chronic syphilis they have no fibrolytic effect on fibrous tissue to allow the spirochaeticidal agents to reach the parasites.

On the other hand, Burke (1935) came to the conclusion that iodides played an important part in the treatment of syphilis in all its stages, and Snodgrass (1935) recommended their use in tertiary lesions. It is generally accepted by those who favour iodides that their beneficial action is in the prevention of excess formation of fibrous tissue and in aiding the resolution of fibrous tissue when formed.

The South African Bantu's normal predilection for the formation of fibrous tissue as evidenced by the frequency of keloids and other entities under the general term of "fibrous diathesis" seemed a good testing ground. In particular, the extensive bone lesions noted in late syphilis in the Bantu, and the dense sclerosis so often seen on x-ray negatives, seemed ideal for evaluating the effects of iodides. Some typical examples of the extensive lesions seen in the Bantu are shown in Figs 1 and 2 (opposite).

Iodides in the Treatment of Syphilis

There is sufficient clinical and experimental evidence to establish the following facts with regard to the iodides :

- (1) *In vitro* the *T. pallidum* is not materially affected by isotonic solutions of sodium and potassium iodide.
- (2) Isotonic solutions of sodium or potassium iodide do not materially affect the number or mobility of *T. pallidum* when applied to a chancre.
- (3) Oral, intravenous, and rectal administration of potassium iodide carried out singly, and in the case of oral and intravenous routes, by combination, for periods of 1 to 3 days do not materially alter the number or mobility of *T. pallidum*.
- (4) Potassium or sodium iodide given by oral, intravenous, or rectal routes for one week have no effect on the treponema content of moist secondary lesions.

* Received for publication December 4, 1952.

FIG. 1.—Active syphilitic osteitis in elbow region. Joint space indicated by arrows.

FIG. 2.—End result of syphilitic osteitis in shoulder girdle. Destruction of shoulder-joint and gross deformity of humerus and scapula.

ably large doses. Most workers recommend a minimum of 90 gr. potassium iodide daily.

The Position in South Africa.—Potassium iodide has always been popular with workers among the Bantu. The general use of arsenicals and bismuth in the Non-European was considerably delayed on account of socio-economic difficulties, and even now is not in as general use as it should be. The teaching of the pioneers who worked in the pre-arsenical days and the native's belief in the "bitter medicine" account for the extensive use of potassium iodide in rural areas.

Modern syphilologists, however, have belittled the use of iodides on experimental grounds, and in the urban clinics, iodides, if used at all, are relegated to the normal Mist. Potassium Iodide in the interval period between courses of arsenicals and bismuth.

The temptation to treat a series of cases with potassium iodide alone was ever present, but was not considered justified from the patient's point of view. As stated by Moore (1941):

The exact evaluation of the worth of iodides in modern syphilotherapy combined as they must be with other powerful antisyphilitic drugs is, to our way of thinking, impossible.

Iodides are therefore used entirely on empirical grounds, but the general impression is that they do

(5) Under the same conditions, there is no evidence of resolution of moist lesions, involution of rashes, or resolution of adenitis.

(6) Potassium iodide given orally can cause the resolution of gummata of the skin.

(7) In tertiary syphilis, pain, sleeplessness, anaemia, and loss of appetite are quickly relieved by iodides alone.

(8) Iodides have no effect on the serological reactions of syphilis.

(9) Iodides probably increase the rate of resolution of tertiary lesions when used in conjunction with the recognised antisyphilitic agents.

(10) To be effective iodides must be given in reason-

play a part in syphilotherapy particularly in the tertiary stage.

For some years it has been the custom in the Out-patient department of the Non-European Hospital, Johannesburg, to treat all cases of bone syphilis showing dense sclerosis with a preliminary course of potassium iodide. This is contrary to the general opinion of syphilologists in South Africa, and in an attempt to assess the position, an analysis was made of a series of cases of bone syphilis treated in the out-patient department. It was found that several cases had been unintentionally treated with potassium iodide alone, and by a set of fortuitous circumstances three of these cases returned to hospital for other reasons at periods varying from 9 months to 24 months, so that it was possible to see the "end-results".

The description of these three cases and of a fourth which gave dramatic results with potassium iodide after arsenical treatment, is the justification of this paper.

Case Reports

Case 1, adult female Bantu, referred to the out-patient department with pains in both legs of several months' duration, worse at night.

The clinical picture was classical of an active syphilitic periostitis in the Bantu: tenderness along both tibial crests; increased heat; slight pitting oedema and minimal constitutional signs.

The Wassermann reaction was strongly positive, and the x-ray photographs showed extensive syphilitic periostitis of both tibiae and fibulae with dense sclerosis.

This patient was referred to the Municipal Venereal Diseases Clinic and received the routine weekly arsenical and bismuth injections for nearly 9 months. At the end of this period she was referred back with the following note:

"Please investigate this case. Her Wassermann is now negative but she still complains of pains in the legs. Is there a double pathology?"

Radiologically there was little change, but clinically the local condition had improved. There was no oedema, no increased heat, and tenderness was minimal. A course of increasing doses of potassium iodide was prescribed and within 2 weeks the patient's symptoms cleared up. At the end of 6 weeks she was symptom free, but the Wassermann reaction had become positive again. Further injections of arsenicals and bismuth finally gave a negative serological reaction in a symptom-free patient.

Case 2, female Bantu, aged 11, complaining of pains in both legs of 2 months' duration. Clinically the picture was much the same as in Case 1. X-ray photographs showed extensive periostitis without undue sclerosis (Fig. 3). The Wassermann reaction was strongly positive.

FIG. 3.—Case 2, before treatment. Note extensive periostitis of both tibia and fibula (arrows). Oedema redness and heat present accompanied by pain and disability of two months' duration.

It was decided to give the patient a preliminary course of potassium iodide. In view of her age, 7½ gr. three times a day were prescribed, and she was given a sufficient quantity to last a week, with instructions to return at weekly intervals. The patient returned 5 weeks later and asked for another bottle of medicine. When asked why she had not returned after a week the reply was: "The medicine made the pains go away and I thought I was cured."

During the next 6 weeks the dosage was gradually increased, and during the last 2 weeks the patient was receiving 45 gr. daily. At this stage she was symptom-free and the radiological pictures showed some improvement (Fig. 4).

The patient was referred to the Municipal Clinic for Venereal Diseases for routine treatment but did not

FIG. 4.—Case 2, 6 weeks after commencement of treatment. Maximum dose 45 gr. potassium iodide daily. Note condensation of periostitis (arrows). Patient now symptom-free.

attend, presumably because she did not realize the necessity. Nearly 10 months later, however, she attended the Ophthalmic department for treatment of a Meibomian cyst. She had no symptoms in the lower limbs, and clinically seemed in good health. She was again referred to the Venereal Diseases Clinic but did not attend.

Comparison of the two radiographs show the marked improvement in the osseous lesions, which followed treatment with potassium iodide.

Case 3, middle-aged Bantu female, complaining of a painful right knee of one year's duration. For the last month the swelling and pain had increased, and she was unable to walk except with the aid of crutches.

Clinically there were marked arthritic changes with synovial thickening predominating. The Wassermann

reaction was strongly positive, and a diagnosis of gummatous synovitis was made. Radiographic examination showed extensive bone changes (Fig. 5). This is a clinical picture not often seen in Europeans but relatively common in the Bantu. Admission to hospital was advised but the patient refused to stay.

As in the previous case a preliminary course of potassium iodide was prescribed. The knee was put in plaster of Paris, and in 3 weeks the patient reached a dosage of 90 gr. potassium iodide daily which was maintained for 7 weeks; 6 weeks after the commencement of treatment the plaster of Paris was removed. There was marked clinical improvement, and she was able to walk with very little pain.

The dosage of potassium iodide was then increased to 120 gr. daily and this was maintained for 4 weeks. At this stage, after 14 weeks' treatment, the patient was able to walk normally and was able to do all her household work without pain in the affected knee. She was then referred to the Venereal Diseases Clinic, for treatment with arsenicals and bismuth, but did not attend.

Five months later she attended for minor injuries following a fall, and the knee was examined. There was clinical evidence of osteo-arthritis, but the patient was quite comfortable wearing a crêpe bandage. The

FIG. 5.—Case 3, gummatous synovitis with bone involvement. One year's history of pain and disability. Patient only able to walk with crutches. Note bone erosion (1) and (2), periostitis (3), and gummatous degeneration (4).

Wassermann reaction was still positive and she was again referred to the Venereal Diseases Clinic, but once again did not attend.

A year later, that is approximately 17 months after treatment, the patient again attended following a fall. The osteo-arthritic signs had increased, but the patient was quite comfortable, and again refused to attend for injections. The x-ray appearance at this stage is shown in Fig. 6. The Wassermann reaction was strongly positive.

FIG. 6.—Case 3, 17 months after treatment with potassium iodide over a period of 14 weeks with maximum dose of 120 gr. daily. Note regeneration of bone (1), osteophyte formation (2), condensation of periostitis (3), and filling in of gummatous area (4).

Case 4, Bantu male, aged 16, complaining of pain in the right elbow region and left forearm. There was considerable swelling over the posterior aspect of the lower end of the humerus with marked disability in the elbow joint. The x-ray appearances and serological tests confirmed the clinical diagnosis of syphilitic periostitis with gummatous degeneration. Fig. 7 shows the x-ray appearance at this stage.

As in the other two cases it was decided to give the patient a preliminary course of potassium iodide. In 3 weeks a daily dose of 90 gr. was reached, and this was maintained for 3 weeks. At this stage the clinical improvement was dramatic and all pain had disappeared, and it was decided to keep up the treatment with

FIG. 7.—Case 4, before treatment. Note extensive periostitis and areas of gummatous degeneration (arrows). Marked disability with pain, swelling, and reaction in the overlying tissues.

potassium iodide. The dosage was increased to 120 gr. daily and maintained for 2 weeks.

At the end of the treatment, clinical examination showed a slight degree of painless enlargement of the lower end of the humerus, with no disability in the elbow joint except for inability to complete extension. The x rays at this stage showed diminution of the translucent areas and condensation of the periostitis. The patient was referred to the Venereal Diseases Clinic but did not attend.

He returned to hospital 9 months later, however, with an injury to the other arm and an x ray showed that the gummatous area had disappeared and he was clinically free from pain and disability, except for incomplete extension (Fig. 8, opposite).

Discussion

As stated earlier, it has been the custom in the out-patient department to treat all cases of tertiary syphilis of bone showing dense sclerosis with a preliminary course of potassium iodide. The

FIG. 8.—Case 4, 9 months after treatment with potassium iodide for 8 weeks with a maximum dosage of 120 gr. daily. Note condensation of periostitis (arrows) and filling in of translucent areas. Patient symptom-free.

Bantu's tolerance for iodides is very good, and in-patients are given 90 gr. daily in three equally-divided doses without any preliminary testing. Out-patients, however, are given 30 gr. daily for one week, and if tolerance is good, the dosage is rapidly stepped up so that at the beginning of the third week the patient is taking 90 gr. daily. No case of intolerance has been noted with 30 gr. daily. A few, usually women, show signs of intolerance with a daily dose of 90 gr., but most adult females can reach 135 gr. daily, and most adult males 180 gr. daily, without discomfort. The earlier toxic signs are increased salivation, metallic taste in the mouth, and coryza. The aim should be to reach the maximum dose in 3 weeks, and to maintain it for 3 weeks. Symptomatic relief occurs early and is often noted during the first week with a dosage of only 30 gr. daily. An interesting feature has been

the increase in the haemoglobin content of the blood and in the number of erythrocytes during the preliminary course with potassium iodide in cases suffering from anaemia associated with tertiary syphilis. The tonic effect of potassium iodide in these cases is very evident, and despite its bitter taste, it is a very popular mixture with the Bantu.

Snodgrass (1935) after extensive experiments in Scotland maintained that 45 gr. daily was sufficient for his cases, but he preferred to give 90 gr. Burke (1935) in England maintained that 90 gr. daily was the minimum effective dose. Our opinion, based entirely on impressions, is that 90 gr. daily for females and 135 gr. daily for males should be the minimum aimed at and that the shortest period of treatment should be 6 weeks.

How iodides act is not material to the opinions expressed in this paper, but it is interesting to note that Jobling and Petersen (1915) stated that there is present in normal blood serum a substance (antiferment or anti-enzyme) which inhibits the proteolytic effects of trypsin. They found that after the administration of iodides, the antitryptic activity of the blood serum of guinea-pigs and human beings was markedly reduced. In granulomatous and necrotic tissue, proteolytic ferments exist, and their action is, in ordinary circumstances, impeded by the antiferments of the blood. According to the interpretation of Jobling and Petersen, iodine neutralizes the antiferment of the blood and permits the action of the proteolytic ferment in the lesion, with the subsequent solution and absorption of necrotic tissue. Burke (1935) based the fibrolytic action of iodides on their property of being able to link themselves to and saturate the lipoids present in excess in the blood of syphilitics :

Iodine has the effect of saturating the lipid radicals, neutralizing their power, permitting the natural enzymes to act and thus enabling absorption of the granulomatous tissue to take place.

It is our opinion that clinical experience with the Bantu has shown that iodides play an important part in the treatment of the dense fibrous and sclerotic lesions of bone seen in the tertiary stage of syphilis in the Negro in South Africa, and that treatment with iodides is beneficial in all cases, and essential in some (see Case 1).

The role of the iodides in the other stages of syphilis is open to discussion. The histological picture of the primary and secondary lesions, with the perivascular infiltration by lymphocytes and plasma cells, with narrowing of the affected blood vessels, is one of the preliminary steps in the formation of fibrous tissue. This would suggest

that iodides should prove beneficial even in the earlier stages as suggested by Burke. The infective nature of the lesions in the earlier stages and the knowledge that iodides are not antispirechaetal, have made experiments impossible, but it is suggested that iodides should be used in conjunction with the recognized antisyphilitic agents in the earlier stages, or alternatively, that an intensive course of iodides should be given between the first and second course of arsenicals and bismuth.

It must be made clear that the views expressed in this paper are based entirely on clinical experience with the Bantu in South Africa. In the Bantu, the secondary stage is more florid, the tertiary lesions are more fibrous and extensive, and the whole clinical picture is more dramatic than in the European.

However, the causal agent is the same and the histo-pathology very similar in both races, and it is suggested that if potassium iodide is beneficial to the Bantu it should prove of benefit in the treatment of similar, if less fibrous, lesions in the European.

Summary

(1) The role of potassium iodide in the treatment of syphilis is discussed.

(2) One case of bone syphilis is described in which potassium iodide apparently played an essential part in the treatment of the condition.

(3) Three cases of bone syphilis, unintentionally treated with potassium iodide alone, are described.

(4) It is suggested that the clinical and radiological evidence in these cases shows that potassium iodide can accelerate the resolution of certain syphilitic lesions.

(5) It is further suggested that a preliminary intensive course of potassium iodide, details of which are given, should be administered to all patients showing dense sclerotic bone lesions.

(6) It is felt that despite modern methods of treating syphilis, potassium iodide is still a useful adjunct in the treatment of bone syphilis, particularly in the Bantu of South Africa.

REFERENCES

- Burke, E. T. (1935). *Arch. Derm. Syph., Chicago*, 32, 404.
 Greenbaum, S. S., and Cobane, J. (1934). *Amer. J. Syph.*, 18, 289.
 Jobling, J. W., and Petersen, W. (1915). *Arch. intern. Med., Chicago*, 15, 286.
 McDermott, W. (1947). In R. L. Cecil, "Textbook of Medicine", 7th ed., pp. 358-387. Saunders, Philadelphia.
 Moore, J. E. (1941). "The Modern Treatment of Syphilis", 2nd ed., p. 164. Thomas, Springfield, Ill.
 Snodgrass, W. R. (1935). *Quart. J. Med.*, n.s. 4, 247